

## **REMARKS**

### **Claim Objections**

Claims 3 and 9 have been revised to refer to "Table 1" instead of "Table I." This error was only recently noticed and could not have been earlier corrected.

### **Claim Rejections – 35 U.S.C. 112, First Paragraph**

#### *Enablement*

Claim 3, 6, 8-15 and 20-22 have been rejected for allegedly failing to comply with the enablement requirement. The Examiner identified this as a new ground of rejection.

The Examiner stated on page 3, last paragraph that "There is no indication in the specification that binding will necessarily change confirmation. How does one determine whether the compound is capable of changing the receptor from active to inactive without performing another step, such as an assay?"

The Applicants submit that amended claim 3 is enabled because it recites the additional method step of determining whether the test compound agonizes insulin receptor activity in an insulin receptor activity assay. Claims 9, 11 and 13 have also been amended to recite a similar step, determining whether the test compound antagonizes insulin receptor activity in an insulin receptor activity assay. Dependent claims 8, 10, 12 and 14, which had referred to an assay have now been cancelled.

The Applicants have also deleted wording in claims 3, 9, 11 and 13 that refers to the ability to change insulin receptor from an active conformation to an inactive conformation or bias insulin receptor toward an inactive conformation. Amended claim 3, for example, now recites comparing structural coordinates of the compound and the ligand binding site and determining whether the compound fits spatially into the ligand binding site.

### **Claim Rejections – 35 U.S.C. 112, First Paragraph**

The Examiner objected to claims 11-15, 21 and 22 which included the term "Cam-loop" segment. The term "Cam-loop" has been deleted and replaced by reference to the range of amino acid residues 250-280, which is discussed on page 51, lines 6-9 of the application. For the Examiner's reference, useful illustration of the Cam-loop is found in the figures (e.g. figures 5-7 and 9) and the application (e.g. pages 25-26, 51 and 55-58).

### **New Claims/Support for Amendments**

Claims 23 and 24 are newly added. Claims 23 and 24 are directed to the methods of claim 11 and 13, respectively where at least one residue between amino acids 250 to 280 is selected from the group consisting of Lys265, Lys267, Asn268, Arg270, Arg271 and Gln272. Support for the newly added claims 23-24 is found in the application under Table 2 on pages 26-27. These additional claims do not require a new search and are fully encompassed within the dependent claims already searched, and Applicant submits are allowable.

In Table 1 (page 23 of application as filed) reference to Glu250 (line 33) has been deleted and replaced with Asp250. Support for this amendment may be found in the application as filed under Figure 12 where amino acid 250 of the IR sequence submitted is “D” which corresponds to aspartic acid.

In Table 1 (page 23 of application as filed), the entry located at line 34 has been deleted.

References to amino acid residues Arg272 and Glu273 have been deleted from Table 2 (pages 26-27 of application as filed).

Amino acid residues Arg271 and Gln272 have been added to Table 2 (pages 26-27 of the application). Support for these additions is found in the application on page 51 which specifies a cam-loop segment ranging from amino acids 250-280 of the insulin receptor sequence. Both of the added amino acid residues fall within the specified 250-280 range.

Amino acid residue Glu6 has been added to Table 2 (page 26 of application as filed) under the “L1 surface near cam-loop segment” heading. Support for this addition is found in the application under the legend for Figure 6 (page 15) which refers to L1 as encompassing amino acids 1-158.

These typographical errors were only recently discovered and thus could not have been earlier corrected.

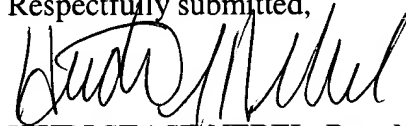
Table 2 (pages 26-27 of original submission) US 09/744,628

Cam-loop segment of Cys-rich region		L1 surface near cam-loop segment	
Lys265	electrostatic	Glu1NH <sub>3</sub> <sup>+</sup>	electrostatic
		Glu6	electrostatic
Lys267	electrostatic	Asn15	polar
Asn268	polar	Asn16	polar
Arg270	electrostatic	Arg19	electrostatic
		Glu22	electrostatic
		Glu24	electrostatic
Arg271	electrostatic	Asn25	polar
Gln272	polar	Glu44	polar
		Asp45	electrostatic
		Arg47	electrostatic
		Asp48	electrostatic
		Lys53	electrostatic

### Conclusion

This is a request to extend the period for filing a response in the above-identified application for three months from August 18, 2004 to November 18, 2004. Applicant is a small entity; therefore, enclosed is our check for \$490.00 to cover the cost of the three month extension. Any deficiency or overpayment should be charged or credited to Deposit Account 26-0084.

Respectfully submitted,



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